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ANEMIA AND GRANULOCYTOPENIA IN RATS FED A DIET LOW IN PANTOTHENIC ACID[1]

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Spicer, Daft, Sebrell, and Ashburn (*1*) reported the development of agranulocytosis or granulocytopenia, bone-marrow hypoplasia, and an occasional anemia in rats given sulfaguanidine or sulfasuxidine (succinyl sulfathiazole) in purified diets. Anemic and granulocytopenic animals were treated successfully with whole dried liver or with certain liver extracts which were known to contain the *L. casei* factor ("folic acid," "vitamin B_c"). Confirmatory results have been presented by other investigators (*2, 3*). Kornberg, Daft, and Sebrell (*4*) described similar blood findings, with a greater incidence of anemia, in rats given sulfadiazine or sulfathiazole. Extracts prepared from liver were again found to be effective in curative experiments. Following the isolation of vitamin B_c by Pfiffner et al. (*5*) and the *L. casei* factor by Stokstad and co-workers (*6, 7*), Daft and Sebrell (*8*) announced the successful use of these crystalline materials in the treatment of sulfonamide-induced blood dyscrasias. Kornberg, Daft, and Sebrell (*9*) noted the development of granulocytopenia in a small percentage of rats given a purified diet without sulfonamide. Treatment with *L. casei* factor corrected this dyscrasia.

We wish to report at this time that a deficiency of pantothenic acid in rats may result in anemia, granulocytopenia, and bone-marrow hypoplasia. In the present series of experiments a large proportion of the deficient animals developed dyscrasias, while the control rats receiving adequate pantothenic acid showed almost no deficiency signs. Despite the manifest effectiveness of pantothenic acid in

[1] From the Division of Physiology and the Pathology Laboratory, National Institute of Health.

[2] A preliminary report on this work was presented by the senior author at the Vitamin Conference, Gibson Island, Md., July 25, 1944.

preventive experiments the results of therapeutic tests indicated that the blood and bone-marrow changes were not manifestations of an uncomplicated deficiency of this vitamin.

DEVELOPMENT OF DYSCRASIAS

Albino rats of the Osborne and Mendel or Wistar strain at weaning or within a week thereafter were placed on one of two similar pantothenic acid-deficient diets. Diet No. 939 consisted of leached and alcohol-extracted casein, 18 percent; Crisco, 8 percent; salt mixture No. 550 (*1*), 4 percent; dextrose (Merck U. S. P.), 69.8 percent; $FeSO_4.7H_2O$, 0.18 percent; and $CuSO_4.5H_2O$, 0.02 percent. Into each 100 gm. of this diet were incorporated 1 mg. of thiamine hydrochloride, 2 mg. of riboflavin, 1 mg. pyridoxine hydrochloride, 2 mg. of niacin, 400 micrograms of vitamin K,[3] 1 microgram of biotin, and 200 mg. of choline chloride. Diet No. 966 differed only in that the niacin, vitamin K, and biotin were omitted. Each rat received a supplement twice weekly of 0.25 cc. of corn oil containing 2,000 units of vitamin A and 200 units of vitamin D (Natola). The rats on diet No. 939 each received in addition a weekly supplement of 3 mg. of α-tocopherol in ethyl laurate.

In some of the litters, one rat was given an additional daily oral supplement of 200 micrograms of pantothenic acid. These animals served as controls. A few rats to be discussed under "Treatment of Dyscrasias" were given pantothenic acid at a level of 2 or 5 micrograms per day or *L. casei* factor [4] at a level of 2 or 20 micrograms per day.

At various times, total white cell counts, polymorphonuclear granulocyte counts, hematocrit determinations, and occasionally total red cell counts and hemoglobin determinations were made on the tail blood of these animals. Hemoglobin was determined by the oxyhemoglobin method of Sanford et al. (*10*) and hematocrits with the Van Allen microhematocrit tube using 1.3 percent sodium oxalate. Polymorphonuclear granulocyte counts were made directly in the counting chamber under a high dry lens (×300). The accuracy of this method was established by numerous checks against differential white cell counts made on smears stained with Wright's stain.

For the purpose of this report we shall use the term "blood dyscrasia" to denote a granulocytopenia or an anemia or both combined; we shall use the term "granulocytopenia" to indicate a total polymorphonuclear granulocyte count of not more than 400 cells per cubic millimeter; and we shall use the term "anemia" to indicate hematocrit values of 35 volumes percent or less. These definitions of granulo-

[3] 2-methyl-1, 4-naphthohydroquinone diacetate.

[4] Fermentation product supplied through the courtesy of Dr. E. L. R. Stokstad and Dr. B. L. Hutchings, of Lederle Laboratories, Inc., Pearl River, N. Y.

cytopenia and anemia are admittedly arbitrary. They were adopted primarily to serve as a basis for selection of animals for treatment.

Some phases of our study of the occurrence of anemia and granulocytopenia in rats on pantothenic acid-deficient diets and of the treatment of these dyscrasias are not as yet concluded. In order to indicate with some degree of accuracy the incidence of the blood changes, we will discuss in this section only completed experiments; i. e., experiments in which all of the deficient animals have developed a dyscrasia or have died. The results to be presented were obtained with 40 groups of rats, each group consisting of litter mates of the same sex. There was a total of 92 rats on which counts were obtained; 69 of the 92 were pantothenic acid-deficient and the other 23 were control animals given supplementary pantothenic acid at a level of 200 micrograms per rat per day.

Of the 92 rats to be considered, 57 (41 deficient animals and 16 controls) received diet No. 939, and 35 (28 deficient animals and 7 controls) received diet No. 966. No significant differences were noted between the groups given these two similar diets and the results obtained therefore have been combined and will be considered together.

The results of the blood counts on control animals are recorded in table 1. In most instances only a single count was made. It cannot be said, therefore, that these represent the lowest counts which might have been obtained on the individual animals. Obvious signs which might be attributed to a dietary deficiency, however, such as loss of weight, developed in only one animal of the series, No. 1 in table 1. This rat had difficulty in eating because of a dental defect, which may account for the loss of weight. It developed a moderate leucopenia and a mild transient anemia. For only one other animal in this group, No. 2, was there observed a total leucocyte count below 10,000 cells per cubic millimeter, a total polymorphonuclear count below 1,000 cells per cubic millimeter, or a hematocrit of less than 39 volumes percent.

Results of blood counts on the 69 pantothenic acid-deficient rats are given in table 2. Only the lowest count obtained on each animal is recorded. Twenty of the 69 rats were both granulocytopenic and anemic; 1 was granulocytopenic only; 27 were anemic only; 21 showed neither dyscrasia. In this particular series, therefore, the incidence of the anemia was much greater than that of the granulocytopenia. In other groups of rats, however, the preponderance of anemia over granulocytopenia was not as great. In a recent incomplete study, for example, we have observed 23 cases of anemia alone, 14 of granulocytopenia alone, and 15 of both together. It is worthy of note that the most severe anemsia have occurred in animals which were also granulocytopenic.

TABLE 1.—*Blood counts on rats given adequate pantothenic acid*

Rat No.	Days on experiment	Total white blood cells per cu. mm.	Polymorphonuclear granulocytes per cu. mm.	Hematocrit volume percent
1	98	13,000	2,000	39.8
	105	4,800	1,200	35.5
	113	7,450	1,150	36.1
	139	5,200	3,700	49.4
2	118	6,750	850	39.9
3	63	15,400	3,100	42.1
4	70	21,100	1,700	42.6
5	107	13,550	2,300	43.2
6	53	15,100	2,200	43.5
7	113	16,850	3,250	43.5
8	27	14,600	2,600	39.2
	98	22,350	1,800	43.7
9	53	16,550	1,100	45.2
10	130	13,100	3,250	45.2
11	99	17,300	3,100	45.4
12	68	11,900	2,800	45.8
13	76	10,850	1,600	46.2
14	130	18,800	5,400	46.4
15	85	12,250	2,450	46.5
16	159	14,100	2,000	46.7
17	63	13,600	1,200	47.1
18	99	16,600	1,650	47.4
19	85	30,000	2,700	47.7
20	33	16,950	1,500	44.1
	104	20,250	1,600	47.9
21	104	10,550	1,500	50.2
22	110	14,550	1,400	51.0
23	186	11,650	1,000	51.4

TABLE 2.—*Blood counts on rats fed a diet deficient in pantothenic acid*

Rat No.	Days on experiment	Total white blood cells per cu. mm.	Polymorphonuclear granulocytes per cu. mm.	Hematocrit volume percent [1]
Rats with granulocytopenia and anemia combined				
24	54	2,500	50	6.0
25	39	1,600	50	6.1
26	39	1,350	0	6.8
27	56	1,400	100	9.9
28	53	1,450	100	10.3
29	28	2,150	100	10.4
30	49	600	50	14.6
31	52	1,750	250	14.7
32	26	1,950	150	16.8
33	41	2,000	0	17.7
34	50	1,600	150	19.0
35	53	1,500	0	23.7
36	42	900	0	25.0
37	39	2,750	0	25.0
38	47	2,050	150	25.1
39	64	950	150	27.1
40	23	250	0	29.5
41	60	900	150	31.7
42	53	2,400	400	31.9
43	47	1,200	400	33.1

[1] The hemoglobin values and red blood cell counts which were obtained are as follows:

Rat number	Hemoglobin in grams per 100 cc.	Total red blood cells millions per cu. mm.	Rat number	Hemoglobin in grams per 100 cc.	Total red blood cells millions per cu. mm.
26	3.0	1.2	49	5.8	3.0
27	4.7	1.9	50	9.8	4.5
31	6.9	2.9	51	6.6	3.3
33	6.6	3.4	55	10.9	6.4
36	10.6	5.0	57	8.2	4.2
38	9.2	4.8	58	11.0	5.0
41	10.5	5.3	60	13.5	7.1
42	12.6	6.3	63	9.4	4.3
47	5.9	3.5			

TABLE 2.—*Blood counts on rats fed a diet deficient in pantothenic acid*—Continued

Rat No.	Days on experiment	Total white blood cells per cu. mm.	Polymorphonuclear granulocytes per cu. mm.	Hematocrit volume percent
Rat with granulocytopenia alone				
44	55	2,750	100	44.3
Rats with anemia alone				
45	68	11,800	9,700	12.2
46	85	8,450	2,100	15.5
47	38	5,600	1,650	15.9
48	31	7,400	5,000	18.1
49	24	13,600	4,600	24.5
50	55	4,150	700	24.8
51	27	17,650	10,150	27.2
52	27	27,200	12,000	27.9
53	89	8,650	3,200	28.0
54	69	5,850	2,700	29.1
55	50	19,800	9,700	29.3
56	38	11,500	5,650	29.6
57	32	9,950	7,100	29.6
58	49	9,000	1,350	29.9
59	24	5,600	2,300	30.2
60	42	4,900	1,400	31.3
61	35	23,450	12,600	31.8
62	43	12,450	2,600	32.1
63	43	4.100	700	32.2
64	95	2,500	1,350	32.9
65	34	17,250	8,450	33.2
66	51	8,500	4,300	33.4
67	35	8,200	5,800	34.0
68	38	3,100	2,900	34.3
69	35	2,800	550	34.7
70	44	6,600	2,400	34.9
71	58	6,500	2,750	35.0
Rats with no defined blood dyscrasia				
72	65	14,800	4,600	35.6
73	71	9,500	2,400	35.9
74	29	5,650	1,500	36.0
75	77	7,000	3,400	36.5
76	62	11,400	4,400	37.1
77	175	8,150	2,700	38.8
78	70	9,600	3,200	39.2
79	24	10,000	800	39.5
80	20	12,600	3,400	39.9
81	56	17,050	1,900	40.0
82	38	----------	----------	41.4
83	46	8,850	4,500	41.8
84	36	7,250	3,600	42.2
85	38	14,400	8,000	43.5
86	29	2,900	1,200	44.3
87	38	----------	----------	44.6
88	36	7,500	950	44.8
89	47	10,000	1,400	45.2
90	69	5.850	3,200	46.3
91	37	3,350	1,000	53.3
92	28	16,450	6,800	54.8

In some rats, the onset of the blood dyscrasias, particularly the anemia, was extremely rapid and was followed closely by a fatal termination of the disease. Rats were examined every day although blood counts were not made as frequently. It was not uncommon to find that a rat's eyes, ears, mucous membranes, and foot pads were bright pink one day and extremely pallid the next. Gross evidences of internal or external hemorrhage or icterus were not present. In table 3 are given a few instances in which counts were obtained prior to the abrupt fall in the level of circulating cells.

TABLE 3.—*Rapidity of development of blood dyscrasias*

Rat No.	Date	Total white blood cells per cu. mm.	Polymorphonuclear granulocytes per cu. mn.	Hematocrit volume percent	Date	Total white blood cells per cu. mm.	Polymorphonuclear granulocytes per cu. mm.	Hematocrit volume percent	Date of death
34	June 7	2,650	600	38.0	June 13	1,250	50	27.5	[2]
36	June 14	6,900	900	38.9	June 20	900	0	25.0	June 22
41	June 20	3,800	1,700	35.1	June 24	900	150	31.7	June 26
47	Apr. 18	10,900	1,650	30.5	Apr. 22	5,600	1,650	15.9	Apr. 24
49 [1]	May 1	11,900	1,550	37.5	May 2	10,250	1,300	26.9	May 4
93	Apr. 22	3,050	850	38.1	Apr. 25	1.100	150	18.2	Apr. 27
94	Mar. 31	----------	----------	35.6	Apr. 2	750	50	22.2	[2]

[1] Previously had been treated successfully with pantothenic acid.
[2] Treated and recovered.

HISTOLOGICAL EXAMINATION OF THE BONE MARROW

Of the 69 rats listed in table 2, the vertebral and femoral bone marrow was studied in 25, 11 from the group showing both granulocytopenia and anemia, 12 from the group showing anemia only, and 2 from the group showing neither. Of the group showing both granulocytopenia and anemia, 10 rats showed hypoplasia of the bone marrow; it was marked in 5, moderate in 3, and slight in 2. The marrow of 1 rat showed no hypocellularity.

The markedly atrophic marrows also showed varying degrees of congestion, focal hemorrhage, and edema. Generally the stroma was loose in texture with very few scattered adult fat cells. In one of these rats the marrow was moderately fatty. Although severely hypoplastic, a few nucleated red cells and granulocytes were present in all marrows, the latter being least common. The nucleated red cells occurred in very small clusters or, more frequently, were evenly scattered throughout the marrow. Granulocytes occurred most often in very small groups in a peripheral location. A very few of these cells were identified as metamyelocytes and segmented forms; most of these were myelocytes or younger forms. Megakaryocytes were not found in any of these marrows.

In marrows showing only slight to moderate cell depletion, the decrease in the number of cells appeared to occur mainly in the granulocytic series and in some cases cells of the erythroid series appeared to be actually increased in number. In such cases of slight to moderate marrow hypoplasia, the congestion was much less than in the advanced cases and hemorrhage and edema usually were absent.

The bone marrow of the rats with anemia only showed atrophy less frequently and less severe than those with both anemia and granulocytopenia. Of the 12 anemic rats studied, the bone marrow of 8 showed no decrease in cellularity. In 3 there was slight atrophy and in 1 the atrophy was of moderate degree.

The marrow of the control rats in this experiment was not studied. Interpretation of the findings in the marrow of the rats on the deficient regimen was made by comparison with marrow sections of control rats of the same strain and age group used in other experiments.

TREATMENT OF DYSCRASIAS

The results to be considered in this section were obtained partly with animals mentioned under "Development of Dyscrasias" (page 1202) and partly with a larger group of similar animals. Some of these animals developed blood dyscrasias while receiving the *L. casei* factor, at a level of 2 or 20 micrograms per rat per day, or pantothenic acid at a level of 2 or 5 micrograms per rat per day. The nature and amount of such supplementation are given, together with the nature and the results of therapy, in tables 4, 5, and 6. Diets No. 939 and No. 966, described in the previous section, were employed throughout.

Treatment consisted of the daily oral administration for 4 days (in a few cases 10 days) of pantothenic acid, fermentation *L. casei* factor (replaced by synthetic *L. casei* factor in a few animals, as noted), or the indicated combination of the two vitamins. Blood determinations were made the day treatment was started, and were repeated, for granulocytopenic rats, at the termination of the 4-day treatment period and, for anemic rats, after the lapse of approximately 6 additional days. Experience has shown that there may be no increase in hematocrit or hemoglobin values or in red cell counts in 4 days, even when treatment for this length of time initiates changes observable at the end of an 8–10-day period.

The fulminating character of the deficiency disease has proved to be a considerable handicap in the accumulation of data concerning therapy. Only a small percentage of treated animals survived the treatment test period. This was true even when the therapeutic measures employed were such as to bring about a correction of the blood dyscrasias in most or all of the animals which lived for the necessary 4 or 8 to 10 days following the beginning of therapy. Because of the difficulty of obtaining adequate therapeutic data, a few animals were treated as granulocytopenic even though the level of circulating granulocytes was slightly above 400 cells per cubic millimeter. We do not feel that it is possible at the present time to evaluate the failure of so many treated animals to survive. In view of the uncertainty concerning the significance of these early deaths we have adopted the procedure of reporting data concerning treatment only for those granulocytopenic animals which survived a 4-day test period and for those anemic animals which lived for at least 8 days from the time treatment was begun.

The results of treatment of anemic animals which were not granulocytopenic are given in table 4. Each of 12 rats treated with panto-

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TABLE 4.—*Anemic rats; changes in blood values following treatment*

Rat No.	Treatment			Hematocrit [1] volume percent				Polymorphonuclear granulocytes per cu. mm.				Weight gain or loss following initiation of therapy, gm./10 days	Remarks
	Panto-thenic acid (micro-grams)	*L. casei* factor (micro-grams)	Days of therapy	Number of days after beginning of treatment [2]									
				0	4	10	16	0	4	10	16		
49	200		4	24	27	31	37	4,600	8,800	1,050	2,650	+3	
51	200		4	27		41		10,150		10,800		+6	
53	200		4	32	28	42		3,700	3,200	3,100		+22	
55	200		4	29	31(6)	39(12)	55(27)	9,700		5,600(12)	13,200(27)	+3	
58	200		4	30		53(8)		1,350				+2(4)	
95	5,000		4	32	34	38	45	1,500	2,400	900	1,400	+36	Received 2 micrograms of pantothenic acid daily from weaning.
96	200		4	29		47		2,700		1,000		+28	
97	200		4	29	33	43(11)		700	1,250	1,350(11)		+30	
98	200		4	25		35	41	3,050		2,000	5,400	+16	
99	200		4	30		41		2,500		400		+18	Further treatment was begun at end of 10-day period. See table 5.
100	200		4	19		39		5,600		100		+28	Do.
101	200		4	33		36		1,750		250		+5	
48		100	4	27	18	18(8)		1,850	5,000			−5(8)	
52		100	4	28	28	42(11)		12,000	7,150	1,250(11)		0	
59		100	4	30	28	34	37(17)	2,300	1,800	6,000	4,050(17)	+1	
102		100	4	21	13(6)	12		1,650		7,100		−3	
103		100	4	31	34	25(11)	27(19)	800	700	400(11)	750(19)	+3	Received 2 micrograms of *L. casei* factor daily from weaning.
104		100	4	29	28	16(9)		8,600	3,200	9,800(9)		−6(9)	Do.
105		100	4	27	22	17		4,150	9,500			+2	Do.
106		25	4	26	29	12		3,400	3,550	36,000		+2	
107		25	4	21	28	43(11)		3,050	2,800	4,850(11)		+5	
108		25	4	33	40	43(8)		2,950	7,800			−3(4)	Synthetic, *L. casei* factor.[3]
109		25	10	21	12	13(9)		2,200	650	2,650(9)		−5(9)	Do.
110		25	4	22	47	49		3,400	2,400	2,000		−6	Received amino acid solution in place of drinking water during treatment period.[4]
111		100	4	27	37	31(11)		1,050	1,250	3,000(11)		+5	Do.
112		100	10	26	19	12(9)		2,800	1,300	0(9)		−4	Do.

113	200	25	4	19	30	42	45 (27)	2,200	6,100	4,850	1,850 (27)	+27	
114	200	25	4	28	41	44	9 (19)	30,000	14,400	2,450	100 (19)	+29	
115	200	25	4	15	35	43	49 (24)	2,000	21,200	1,600	1,000 (24)	+20	
116	200	25	4	22	34	62	----------	2,150	19,600	200	50 (13)	+8	Further treatment was begun at end of 13-day period. See table 5.
117	200	25	4	31	----------	48 (11)	----------	9,600	----------	16,000 (11)	----------	+21	
118	200	25	4	25	29	35 (11)	36 (15)	700	2,350	50 (11)	100 (15)	−7	
119	200	25	4	32	26	28	----------	1,750	----------	50	----------	+6	Further treatment was begun at end of 10-day period. See table 6.

[1] The hemoglobin values and red blood cell counts which were obtained are as follows:

Rat No.	Hemoglobin in gm. per 100 cc.				Total red blood cells, millions (per cu. mm.)				Rat No.	Hemoglobin in gm. per 100 cc.				Total red blood cells, millions (per cu. mm.)			
	0	4	10	16	0	4	10	16		0	4	10	16	0	4	10	16
49	5.8	6.3	7.4	10.3	3.0	----------	3.4	4.1	106	6.6	7.0	2.2	----------	3.1	3.3	1.0	----------
51	6.6	----------	13.0	----------	3.3	----------	5.3	----------	107	5.2	7.0	12.4 (11)	----------	2.2	3.6	4.5 (11)	----------
55	10.9	----------	11.4 (12)	----------	6.5	----------	4.2 (12)	----------	116	4.1	7.5	----------	----------	2.0	5.1	----------	----------
58	11.0	----------	----------	----------	5.0	----------	----------	----------	117	9.3	----------	14.0 (11)	----------	----------	----------	----------	----------

[2] Except where different number of days is indicated by figure in circle.
[3] Furnished through the courtesy of Dr. E. L. R. Stokstad of Lederle Laboratories, Inc., Pearl River, N. Y.
[4] Amino-acid mixture Vx of Bassett et al. (*11*). 100 gm. were dissolved in water and made to a volume of 2,000 ml.

thenic acid showed some increase in the hematocrit reading in approximately 10 days although only 6 of the 12 reached a level as high as 40 volumes percent at this time. Of the 6 which failed to reach this value at 8 to 12 days, 4 reached levels of 37, 41, 45, and 55 volumes percent at 16, 16, 16, and 27 days, respectively, from the beginning of treatment. The other 2 (rats No. 100 and No. 101) became granulocytopenic during the 10-day test period and were subsequently treated with additional pantothenic acid.[5] One (No. 101) succumbed on the thirteenth day before another blood examination was made; the other remained granulocytopenic and became very anemic before it died on the twenty-third day (see table 5, rat No. 100). Of the 14 animals[6] treated with *L. casei* factor, 4 reached hematocrit levels above 40 volumes percent in 4 to 11 days, one appeared to respond slowly reaching a level of 37 volumes percent in 17 days, and the other 9 failed to respond. Of 7 rats treated with pantothenic acid and *L. casei* factor combined, 5 reached hematocrit levels above 40 volumes percent in 4 to 11 days; 1 gave a smaller response, and 1 failed to respond.

The results of therapy of granulocytopenic animals which were not anemic are given in table 5. Fourteen[7] such animals were treated with the *L. casei* factor, 7 were treated with pantothenic acid, and 6 were treated with a combination of the two. Of the 14 treated with the *L. casei* factor alone, 10 gave good responses in 4 days. The 4 which failed to respond became anemic during the treatment period.[8] Three of these died before additional counts were made; the other (No. 32) showed a delayed response. Of the 7 rats treated with pantothenic acid alone, none responded in 4 days or 10 days but 3 of the 4 which lived for more than 16 days finally did respond. Treatment with both vitamins together gave results similar to treatment with *L. casei* factor alone. Three of the six gave good responses in 4 days; 1 responded poorly (an increase to 650 from 0 granulocytes per cubic millimeter) and 2 failed to respond. The 3 which failed to show a good response in 4 days became anemic during the treatment period. Two of these died before additional counts were made; the other (No. 140, treated for 10 days) showed a delayed response.

The results of treatment of animals which were both anemic and granulocytopenic are given in table 6. Six rats[9] were treated with the *L. casei* factor alone, five with pantothenic acid alone, and six

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[5] Rat No. 99 also became granulocytopenic during the 10-day test period. It was treated successfully with additional pantothenic acid as indicated in table 5.

[6] Three of these fourteen received amino acids during the treatment period. See footnote 9.

[7] Six of these fourteen received amino acids during the treatment period. See footnote 9.

[8] Two of the ten which responded also became anemic during treatment.

[9] Two of these six animals received amino acids during the treatment period. (Compare footnotes 6 and 7 and see tables 4, 5, and 6). This procedure did not appear to affect the results which are therefore included. The use of amino acids in the therapy of granulocytopenic animals is under investigation.

TABLE 5.—*Granulocytopenic rats; changes in blood values following treatment*

Rat No.	Treatment: Panto-thenic acid (micro-grams)	Treatment: *L. casei* factor (micro-grams)	Treatment: Days of treat-ment	Total white blood cells per cu. mm.: 0	4	10	16	Total polymorphonuclear granulocytes per cu. mm.: 0	4	10	16	Red blood cell volume (hematocrit) in cc. per 100 cc.: 0	4	10	16	Weight gain or loss following initiation of therapy gm./10 days	Remarks
				Number of days after beginning of treatment [1]													
120	-------	100	4	4,500	6,200	4,900(11)	-------	450	2,250	1,850(11)	-------	42	41	37(11)	-------	+1	Received 2 micrograms of *L. Casei* factor daily from weaning.
121	-------	100	4	2,350	7,350	-------	8,600	350	2,350	-------	4,150	40	37	-------	42	−3(4)	
122	-------	25	4	5,900	11,150	9,550	-------	150	2,800	5,600	-------	42	34	34	-------	−7	Do.
123	-------	25	4	5,000	5,700	2,750	-------	300	1,550	1,050	-------	39	42	40	-------	+3	Do.
32	-------	25	4	1,950	2,350	30,600	13,550	150	400	15,900	2,450	40	17	22	40	−5	—
124	-------	25	4	900	550	-------	-------	100	0	-------	-------	49	34	-------	-------	-------	
40	-------	25	4	650	250	-------	-------	50	0	-------	-------	37	29	-------	-------	−5	—
125	-------	25	4	2,500	600	-------	-------	400	0	-------	-------	37	25	-------	-------	−5(4)	Do.
126	-------	25	4	2,800	3,400	-------	-------	100	2,100	-------	-------	37	24	-------	-------	−2(4)	Received amino-acid solution in place of drinking water during treatment period. See footnote 3, table 4.
127	-------	25	4	2,500	10,100	4,150(8)	-------	50	4,300	1,450(8)	-------	46	42	39(8)	-------	−6(4)	Do.
128	-------	25	4	3,350	7,550	10,100	-------	200	2,150	2,550	950	41	44	41	24	−5	Do.
129	-------	100	4	950	3,000	5,150(12)	-------	200	1,250	2,900(12)	-------	39	39	32(12)	-------	−2	Do.
130	-------	100	4	3,700	6,850	650(12)	-------	50	2,300	0(12)	-------	43	45	19(12)	-------	0	Do.
131	-------	100	4	3,000	18,000	17,800(8)	-------	250	11,200	8,200(8)	-------	42	45	27(8)	-------	−7(4)	Do.
90	5,000	-------	4	2,800	2,450	3,250	9,250(26)	400	500	600	4,650(26)	41	43	44	51(26)	+21	Had been successfully treated for anemia. See table 4.
132	5,000	-------	4	3,600	2,100	4,600	5,550(20)	50	150	400	1,950(20)	41	40	38	37(20)	+12	
44	200	-------	4	2,850	3,300	2,750	4,400(17)	350	550	100	1,450(17)	38	40	44	44(17)	+16	
133	5,000	-------	4	4,450	4,350	4,250	3,900(26)	200	0	0	0(26)	50	33	37	39(26)	+19	
100	5,000	-------	4	1,150	850	1,200	-------	100	100	150	-------	39	17	6	-------	−16	Do.
134	200	-------	4	1,050	350	-------	-------	50	0	-------	-------	36	17	-------	-------	+8(4)	
135	200	-------	4	2,500	1,900	-------	-------	350	200	-------	-------	41	42	-------	-------	0(4)	
136	200	25	4	1,450	53,800	31,700(9)	650(26)	150	50,500	5,100	0(26)	39	39	36	21(26)	+1	
137	200	25	4	2,100	15,700	-------	-------	550	12,400	-------	-------	47	40	-------	-------	−1(4)	
116	200	25	-------	350	7,400	-------	-------	0	4,800	-------	-------	62	53	-------	-------	+1(4)	Do.
138	200	25	4	600	2,350	-------	-------	0	650	-------	-------	40	30	-------	-------	−4(4)	
139	200	25	4	150	300	-------	-------	0	50	-------	-------	42	27	-------	-------	0(4)	
140	200	25	10	350	750	2,700	8,000	50	0	500	5,400	42	32	29	41	+16	

[1] Except where different number of days is indicated by figure in circle.

TABLE 6.—*Treatment of rats which were both anemic and granulocytopenic: Changes in blood values*

Rat No.	Treatment			Total white blood cells per cu. mm.			Total polymorphonuclear granulocytes per cu. mm.			Red blood cell volume [1] (hematocrit) in cc. per 100 cc.			Weight gain or loss following initiation of therapy grams/10 days	Remarks
	Pantothenic acid (micrograms)	*L. casei* factor (micrograms)	Days of treatment	Number of days after beginning of treatment [2]										
				0	4	10	0	4	10	0	4	10		
25		100	4	2,250	1,600		150	50		34	26	6(8)	0(4)	
27		25	4	2,450	700	1,400	50	50	100	35	21	10	−5	
30		25	4	2,150	3,100	600(8)	400	250	50(8)	27	24	15(8)	−2(4)	
141		25	4	1,500	1,400		50	150		34	9		−5(4)	Received 2 micrograms of *L. casei* factor daily from weaning.
142		100	4	3,100	1,400		0	50		31	6		−10(4)	Received amino-acid solution in place of drinking water during treatment period See footnote 3, table 4.
143		100	4	850	200		50	0(8)		31	35(8)		−10(8)	Do.
144	5,000		4	6,250	65,600	9,600	450	2,450	3,400	21	24	42	+28	
145	5,000		4	1,350	1,300	4,900	100	50	2,900	33	31	44	−6	
146	5,000		4	1,750	4,000	5,550	450	850	1,250	29	35	42	+28	
35	200		4	1,350	1,500		50	0		25	24		+17(4)	
147	5,000		4	1,850	450		100	0		33	17		+3(4)	
119	200	25	4	1,600	25,200	4,050	50	17,600	1,450	28	35	31	−3	Had been unsuccessfully treated for anemia. See table 4.
94	200	25	4	750	5,050	4,950(14)	50	1,650	2,250(14)	22	42	55(14)	+19	
148	200	25	4	800	1,000	5,400	0	350	3,550	26	19	35	−6	
38	50	5	4	2,050	4,300	6,050	150	1,300	800	25	37	40	+31	
34	50	5	4	1,250	1,600	3,850	50	150	2,350	28	19	38	+6	
149	200	20	4	400	750	4,850(11)	0	400	1,550(11)	25	27	42(11)	+20	Received 20 micrograms of *L. casei* factor daily from weaning.

[1] The hemoglobin values and red blood cell counts which were obtained are as follows:

Rat No.	Hemoglobin in gm. per 100 cc.		Total red blood cells, millions per cu. mm.		Rat No.	Hemoglobin in gm. per 100 cc.		Total red glood cells, millions per cu. mm.	
	0	10	0	10		0	10	0	10
27	13.4	4.7	7.0	1.9	38	9.2	12.8	4.8	6.7
138	11.8		7.0		34	10.5	12.2	6.8	5.7
35	10.4		5.6		145	9.0	13.3(11)	4.4	5.4(11)
94	6.7								

[2] Except where different number of days is indicated by figure in circle.

with both of these vitamins together. None of the six rats treated with the *L. casei* factor responded either by an increase in the level of circulating granulocytes or by an increase in the hematocrit reading. Of the five treated with pantothenic acid, one showed a good granulocyte response at 4 days and two others at 10 days. The remaining two failed to respond at 4 days and died before another count was obtained. The three animals which lived for 10 days showed increases in the hematocrit values. Of the six animals treated with a combination of *L. casei* factor and pantothenic acid, each gave a good granulocyte response in 4 to 11 days. Hematocrit responses to some extent paralleled the granulocyte responses but were less consistent.

DISCUSSION

In these experiments, anemia and granulocytopenia have developed in rats deprived of pantothenic acid. Nevertheless these dyscrasias appear not to have been signs of an uncomplicated deficiency of this vitamin.

The granulocytopenia, when unaccompanied by anemia, probably was a sign simply of an *L. casei* factor deficiency. This deficiency may have been present in some anemic animals as well. The prophylactic administration of pantothenic acid appears to have prevented the development of an *L. casei* factor deficiency; its therapeutic administration may at times have corrected this deficiency.

The blood dyscrasias observed in rats deprived of pantothenic acid were not ascribable solely to an *L. casei* factor deficiency. The development of anemia appears to have indicated (perhaps with less than complete reliability) the presence of a deficiency affecting hematopoiesis other than that of the *L. casei* factor.

This other deficiency affecting hematopoiesis may have been that of pantothenic acid. There is little or no evidence at hand to the contrary. However, we have seen that the uncomplicated granulocytopenia which occurred in some pantothenic acid-deficient rats was attributable to a deficiency, not of pantothenic acid, but of quite another vitamin. It is possible that a similar mechanism was operative in the appearance of the anemia, with the difference that instead of, or in addition to, *L. casei* factor deficiency there developed a deficiency of an unidentified vitamin. We are unable to state at this time whether the relationship between pantothenic acid and *L. casei* factor deficiencies represents an isolated phenomenon or whether something of general significance is involved.

The discussion of the interpretation of these experimental results would not be complete without mention of three additional points:

1. Most of the *L. casei* factor we have used is a fermentation product. We have no reason to believe that the activity of liver *L. casei* factor

would have been qualitatively different in these experiments but it is a possibility to be considered.

2. It is well known that some degree of inanition accompanies pantothenic acid deficiency in rats. Preliminary investigations of the possible influence of lowered food intake on the development of blood dyscrasias have been carried out (*12*).[10] It appears probable, on the basis of the information at present available, that inanition influences the level of circulating granulocytes but not to an extent sufficient to account for the incidence and the severity of the granulocytopenia observed in pantothenic acid-deficient rats.

3. From inspection of blood smears, it appears that some of our pantothenic acid-deficient rats have infections of *Bartonella muris* (*13*). We have not found it possible, however, to correlate the presence or the severity of the infection with the presence or severity of the anemia.

The syndrome we have described may be identical with the panmyelophthisis of György, Goldblatt, Miller, and Fulton (*14*). We have not studied platelets but the remainder of the blood picture corresponds very well with their findings. The bone-marrow changes in our rats are similar to, though generally less severe than, those described by György et al. On the other hand, these investigators stated that panmyelophthisis was not cured or prevented by a "supposedly active filtrate factor preparation." Since all active "filtrate factor" preparations presumably contained pantothenic acid this observation might be taken as indicating a lack of identity of the deficiency states observed in the two laboratories. Additional information is needed on this point.

SUMMARY

Rats given certain purified diets which were low in pantothenic acid developed anemia, leucopenia, granulocytopenia, and bone-marrow hypoplasia.

The inclusion of pantothenic acid in these diets almost completely prevented the appearance of these deficiency signs.

Therapy with pantothenic acid was much less successful than was prophylaxis. Anemic animals appeared to respond to this treatment somewhat more consistently and rapidly than did those which were granulocytopenic.

[10] Twenty-two pairs of rats have been studied in an experiment involving paired feeding. One rat of each pair was given pantothenic acid-deficient diet No. 966; the other was allowed the same amount of a diet which differed only in that it contained 2 mg. of calcium pantothenate per 100 gm. of diet. Eight of the pantothenic acid-deficient rats were observed with levels of circulating polymorphonuclear granulocytes of 400 cells per cubic millimeter or less (of these 8, 7 were below 200). In addition, 3 animals showed levels between 400 and 1,000. Four of the pair-fed litter mates which received pantothenic acid were observed with levels of circulating polymorphonuclear granulocytes of 400 cells per cubic millimeter or less (none below 200). In addition, 7 rats showed levels between 400 and 1,000.

Evidence is presented which indicates that one result of withholding pantothenic acid from these experimental animals was the development of an *L. casei* factor deficiency.

The nature of the additional deficiency or deficiencies is discussed.

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TSUTSUGAMUSHI DISEASE (SCRUB TYPHUS). THE EFFECTS OF AN IMMUNE RABBIT SERUM IN EXPERIMENTALLY INFECTED MICE [1]

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Immune rabbit serum has been described for several of the rickettsial agents (*1, 2*). The immune serum for Rocky Mountain spotted fever has had a clinical trial and, although the series of cases was not

[1] From the Division of Infectious Diseases, National Institute of Health. This paper was approved for publication May 9, 1944, and scheduled for publication in Public Health Reports in the issue of May 26, 1944. Because of the subject matter the paper was withheld from publication at that time.

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large, the results seemed to warrant the use of the serum as a therapeutic agent in this disease (*3*). As in other diseases, there was evidence that the serum, to be of benefit, must be given in adequate doses as early as possible in the course of illness. In Rocky Mountain spotted fever the diagnosis can only be suspected until the diagnostic rash appears, usually late in the third or early in the fourth day of the febrile period; a definite reduction in the expected case-fatality rates occurred only in those cases where the serum was administered on or before the third day of the rash.

From a clinical standpoint, tsutsugamushi disease might lend itself more readily to therapy and even perhaps prophylaxis with an immune serum than does Rocky Mountain spotted fever. There is observed fairly constantly in tsutsugamushi, at least as it occurs in the white race, an eschar or initial lesion present at the onset of the febrile period (*4*). Cases of the disease have occurred in which the initial lesion was observed by the patient some days before the onset of the febrile period (*5, 6*). With the eschar as an early diagnostic feature, the disease may be recognized very early in its course. It would seem that the earlier the recognition the better the chances that an immune serum or some other therapeutic agent would be of benefit. Two chemotherapeutic agents, para-sulphonamido-benzamidoxime hydrochloride (*7*) and penicillin, were tried in infected white mice but there was no evidence of a favorable effect (*8, 9*).

PREPARATION OF IMMUNE RABBIT SERUM

An immune rabbit serum has been prepared, and in preliminary trials in infected laboratory mice the effect has been sufficient to warrant a brief note. Injection of yolk-sac material infected with the "Karp" strain of tsutsugamushi was begun in four rabbits December 16, 1943. On 2 consecutive days each week for 3 weeks the rabbits received 1 cc. intravenously of a 10^{-1} dilution of a pool of infected yolk sacs that consistently killed white mice when 0.5 cc. of a 10^{-4} dilution was inoculated intraperitoneally. Nineteen days after the last of these six injections the rabbits were bled (January 19, 1944). The serums were separated from the clots and kept in the refrigerator. These serums were tested for complement-fixing antibodies. It was found that one of the rabbits, No. 185, had developed slightly higher fixation with the specific antigen than the others. Serum of this rabbit was used in a preliminary test in mice. After a rest period of several weeks the rabbits were again injected with infectious material (February 14, 1944). The first injection after the rest period was given subcutaneously; the next day an intravenous injection was given; the following week two intravenous injections were given on consecutive days. After approximately 18 days, the rabbits were

again bled for serum (March 9, 1944). The serum from the same rabbit was again tested in infected mice.

INFECTIOUS INOCULUM FOR MICE

Two yolk sacs weighing 8 gm., infected with the "Karp strain," were ground in a blender and then diluted with 80 cc. of sterile skimmed milk (approximately 10^{-1}). This material was then distributed in convenient-sized ampules, shell-frozen rapidly, and stored at approximately $-40°$ C. When this material was thawed and 0.5 cc., in dilutions up to and including 10^{-4}, inoculated intraperitoneally into white mice, they died consistently. An occasional death occurred at 10^{-5}. It therefore appeared that 0.5 cc. of a 10^{-4} dilution contained between 1 and 10 minimal lethal doses for white mice. Dilutions of this pool of frozen infectious material were used throughout the tests of the homologous immune serum in mice.

PROCEDURE

White mice were inoculated intraperitoneally with 0.5 cc. of tenfold dilutions of the infectious pool. At varying periods following inoculation each of the treated mice received a single subcutaneous injection of 0.2 cc. of the crude unpreserved immune rabbit serum. Table 1 summarizes the results obtained with the serum of January 19, 1944, from rabbit No. 185. All deaths which occurred during a period of 40 days are recorded, regardless of cause of death. It will be noted that there was definite delay in the time of death in the treated mice infected with 10^{-3} and 10^{-4} dilutions. There were also some survivors in the 10^{-4} dilution group.

Serum from the same rabbit, No. 185, but from a bleeding following another series of injections with live antigen, March 9, 1944, was tested similarly in mice. The infectious dose was 0.5 cc. intraperitoneally of 10^{-3} and 10^{-4} dilutions from the frozen pool. All deaths that occurred during an observation period of 40 days are recorded in table 2. It will be noted in this table that a very definite effect was produced by the immune serum when given for as long as 72 hours after the 10^{-3} infectious dose and for 120 hours after the 10^{-4} dose of the infectious pool. The serum dosage in this test was kept at the 0.2-cc. amount as it was in the first test.

It was thought that perhaps a little larger dose might be effective when given at a later time after infection of the mice. Table 3 records the results with 0.5 cc. immune serum when mice are infected with 0.5-cc. amounts of 10^{-3} and 10^{-4} dilutions from the Karp infectious pool. As indicated in the table, the mice were observed for 30 days. The effect was obtained as late as 7 days in both the 10^{-3}- and 10^{-4}-dilution infected mice with the larger serum dosage.

TABLE 1.—*Results following inoculation of mice with tsutsugamushi-infected yolk sac (Karp strain) followed by injection of 0.2 cc. immune rabbit serum. Immune serum obtained from rabbit No. 185, bleeding of January 19, 1944*

Number of mice	Infectious dose, Karp yolk-sac pool, 0.5 cc.	Hours after infectious dose 0.2 cc. immune serum was given	Deaths, by days after infection																															Total deaths	Number of survivors
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31–40		
4	10^{-2}	18											2	1					1															4	0
4	10^{-2}	48									2	1		1																				4	0
4	10^{-2}	90									1		1	1						1														4	0
4	10^{-2}	120								1	3																							4	0
4	10^{-2}	No immune serum								2	1	1																						4	0
4	10^{-3}	18														1				1			1											3	1
4	10^{-3}	48															1	1			1											1		4	0
4	10^{-3}	90															1	2		1														4	0
4	10^{-3}	120										1	1	1																			[1]1	4	0
4	10^{-3}	No immune serum									1	1	1		1																			4	0
4	10^{-4}	18																	1													1		2	2
4	10^{-4}	48														1						1												2	2
4	10^{-4}	90								1									2															3	1
4	10^{-4}	120																														2	[1]1	3	1
4	10^{-4}	No immune serum												1	1	1					1													4	0

[1] Dead on fortieth day.

TABLE 2.—*Results following inoculation of mice with tsutsugamushi-infected yolk sac (Karp strain) followed by injections of 0.2 cc. immune rabbit serum. Immune serum obtained from rabbit No. 185, bleeding of March 9, 1944*

Number of mice	Infectious dose, Karp yolk-sac pool, 0.5 cc.	Hours after infectious dose 0.2 cc. immune serum was given	Deaths, by days after infection																															Total deaths	Number of survivors
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31–40		
4	10^{-3}	24				1																												1	3
4	10^{-3}	72																	1															1	3
4	10^{-3}	120												1		2	1																	4	0
4	10^{-3}	192									1	1	2																					4	0
4	10^{-3}	No immune serum									1		1	1		1																		4	0
4	10^{-4}	24																												1				1	3
4	10^{-4}	72																															[1]1	1	3
4	10^{-4}	120														1			1															2	2
6	10^{-4}	No immune serum												1		5																		6	0

[1] Dead on thirty-fifth day.

TABLE 3.—*Results following inoculation of mice with tsutsugamushi-infected yolk sac (Karp strain) followed by injection of 0.5 cc. of immune rabbit serum. Immune serum obtained from rabbit No. 185, bleeding of March 9, 1944*

Number of mice	Infectious dose, Karp yolk-sac pool, 0.5 cc.	Hours after infectious dose 0.5 cc. immune serum was given	Deaths, by days after infection: 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	Total deaths	Number of survivors
4	10^{-3}	72																															0	4
4	10^{-3}	168										1		1																			2	2
4	10^{-3}	No immune serum										1	2	1																			4	0
4	10^{-3}	No immune serum										1	1				1		1														4	0
4	10^{-4}	96																			1												1	3
[1]3	10^{-4}	168																			[2]1												1	2
5	10^{-4}	No immune serum															2	1	1					1									5	0
4	10^{-4}	No immune serum																2		1		1											4	0

[1] Due to shortage of serum, 2 mice treated 0.5 cc. serum; 1 mouse (Blue) treated 0.3 cc. serum. The fourth mouse in this jar untreated and placed in next jar with controls.
[2] Blue.

TABLE 4.—*Results following inoculation of mice with tsutsugamushi-infected yolk sac (Karp strain) followed by injection of 0.2 cc. of immune rabbit serum. Immune serum obtained from rabbits Nos. 13, 186, and 187, bleeding of March 9, 1944*

Immune serum from rabbit No. —	Number of mice	Infectious dose, Karp yolk-sac pool, 0.5 cc.	Hours after infectious dose 0.2 cc. immune serum was given	Deaths, by days after infection: 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	Total deaths	Number of survivors
13	4	10^{-4}	24																	1					1	1								3	1
	4	10^{-4}	72																						1		1							2	2
	4	10^{-4}	168													1		1	1						1									4	0
186	4	10^{-4}	24											1																				1	3
	4	10^{-4}	72																															0	4
	4	10^{-4}	168															1	1								1							3	1
187	4	10^{-4}	24																															0	4
	4	10^{-4}	72																1															1	3
	4	10^{-4}	168														1					1	1											3	1
	4	10^{-4}	No immune serum													1					1	1			1									4	0

Since all the previously described tests were done with the serum from only one (No. 185) of the four rabbits, a test was made with the other three rabbit serums (Nos. 13, 186, and 187). The mice were infected with 0.5 cc. of a 10^{-4} dilution of the Karp infectious pool. They were treated at varying periods later with 0.2 cc. of serum secured from the rabbits in a bleeding of March 9, 1944 (after two series of live-antigen inoculations). The results of this test are summarized in table 4. It will be noted that the serum from rabbit No. 13 was apparently not as efficient as that from No. 186 or No. 187. These two produced a result comparable to that observed with the serum of rabbit No. 185.

DISCUSSION AND SUMMARY

It has been demonstrated that rabbits suitably inoculated with live antigen from a strain of tsutsugamushi (scrub typhus) develop protective antibodies. A second series of inoculations apparently raises the protective antibody titre. These antibodies can be passively transferred to mice previously infected with certainly lethal doses of yolk-sac material from the homologous strain. Death can be prevented in these infected mice, when treated with the serum, after a lapse of 72 to 168 hours from the time of infection. In these tests it appeared that the larger dose was more effective than was the smaller.

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INCIDENCE OF HOSPITALIZATION, AUGUST 1945

Through the cooperation of the Hospital Service Plan Commission of the American Hospital Association, data on hospital admissions among members of Blue Cross Hospital Service Plans are presented monthly. These plans provide prepaid hospital service. The data cover hospital service plans scattered throughout the country, mostly in large cities.

Item	August 1944	August 1945
1. Number of plans supplying data	74	81
2. Number of persons eligible for hospital care	13,670,371	18,499,662
3. Number of persons admitted for hospital care	133,758	176,672
4. Incidence per 1,000 persons, annual rate, during current month (daily rate×365)	115.5	112.4
5. Incidence per 1,000 persons, annual rate for the 12 months ended August 31, 1945	105.1	105.5
6. Number of plans reporting on hospital days	20	31
7. Days of hospital care per case discharged during month [1]	6.13	7.61

[1] Days include entire stay of patient in hospital whether at full pay or at a discount.

DEATHS DURING WEEK ENDED SEPTEMBER 15, 1945

[From the Weekly Mortality Index, issued by the Bureau of the Census, Department of Commerce]

	Week ended Sept. 15, 1945	Corresponding week, 1944
Data from 91 large cities of the United States:		
Total deaths	8,173	7,737
Average for 3 prior years	7,818	
Total deaths, first 37 weeks of year	330,517	332,323
Deaths, under 1 year of age	621	596
Average for 3 prior years	587	
Deaths under 1 year of age, first 37 weeks of year	22,308	22,724
Data from industrial insurance companies:		
Policies in force	67,276,041	66,723,794
Number of death claims	11,251	12,797
Death claims per 1,000 policies in force, annual rate	8.7	10.0
Death claims per 1,000 policies, first 37 weeks of year, annual rate	10.3	10.1

PREVALENCE OF DISEASE

No health department, State or local, can effectively prevent or control disease without knowledge of when, where, and under what conditions cases are occurring

UNITED STATES

REPORTS FROM STATES FOR WEEK ENDED SEPTEMBER 22, 1945

Summary

Following a rise last week, the incidence of poliomyelitis for the country as a whole again declined. A total of 864 cases was reported currently, as compared with 963 last week (the highest weekly incidence to date this year), 1,158 for the corresponding week last year, and a 5-year median (1940–44) of 796. Decreased incidence was recorded in the Middle Atlantic, West Central, and Mountain areas, while increases occurred in the New England, East Central, South Atlantic, and Pacific areas. Of 25 States reporting 10 or more cases, 11 reported a net increase of 83 cases, 12 a decrease of 183, and 2 States, Virginia and Utah, reported the same numbers for both weeks (19 and 22, respectively). States reporting more than 15 cases each are as follows (last week's figures in parentheses): *Increases*—Massachusetts 51 (45), Ohio 37 (31), Illinois 93 (66), Wisconsin 48 (39), Tennessee 21 (15), California 54 (46); *decreases*—New York 110 (148), New Jersey 55 (87), Pennsylvania 48 (95), Minnesota 23 (25), Texas 39 (44), Washington 20 (25). Missouri also reported a decrease from 24 to 9 cases. To date this year 8,883 cases have been reported, as compared with 13,570 for the same period last year and a 5-year median of 5,803.

Of a total of 83 cases of meningococcus meningitis reported for the current week, as compared with 93 last week and 73 for the next earlier week, 14 occurred in New York and 11 in California. The seasonal low was probably reached during the week ended September 1, when 61 cases were reported. The total for the year to date is 6,578, as compared with 13,729 and 14,331, respectively, for the corresponding periods of last year and 1943, and a 5-year median of 2,623.

Of 31 cases of infectious encephalitis reported currently, 24 occurred in California, which State has reported 204 of the total of 455 cases to date this year.

A total of 8,205 deaths was recorded for the week in 93 large cities of the United States, as compared with 8,238 last week, 8,027 for the corresponding week last year, and a 3-year (1942–44) average of 8,049. The total to date is 341,548, as compared with 343,526 for the corresponding period last year.

Telegraphic morbidity reports from State health officers for the week ended September 22, 1945, and comparison with corresponding week of 1944 and 5-year median

In these tables a zero indicates a definite report, while leaders inply that, although none was reported, cases may have occurred.

Division and State	Diphtheria			Influenza			Measles			Meningitis, meningococcus		
	Week ended—		Median 1940–44	Week ended—		Median 1940–44	Week ended—		Median 1940–44	Week ended—		Median 1940–44
	Sept. 22, 1945	Sept. 23, 1944		Sept. 22, 1945	Sept. 23, 1944		Sept. 22, 1945	Sept. 23, 1944		Sept. 22, 1945	Sept. 23, 1944	
NEW ENGLAND												
Maine	2	1	0	1	------	------	1	3	10	0	3	1
New Hampshire	0	0	0	------	------	------	0	3	0	0	0	0
Vermont	2	0	0	------	------	------	0	2	2	0	0	0
Massachusetts	4	3	4	------	------	------	41	26	31	[3] 2	1	3
Rhode Island	0	0	0	15	2	------	1	0	0	0	1	0
Connecticut	0	1	1	------	1	1	0	6	6	0	2	0
MIDDLE ATLANTIC												
New York	11	10	7	[1] 2	([1])	[1] 2	11	17	43	14	13	5
New Jersey	4	4	3	------	------	2	6	9	32	5	5	2
Pennsylvania	5	5	7	2	------	------	32	51	51	3	8	4
EAST NORTH CENTRAL												
Ohio	6	7	6	2	------	4	14	5	14	4	3	1
Indiana	9	4	9	2	4	12	2	2	10	4	1	1
Illinois	1	6	10	------	4	4	32	8	19	2	11	2
Michigan [2]	20	3	1	1	2	2	35	13	22	1	4	2
Wisconsin	2	0	0	12	12	14	20	21	34	0	3	2
WEST NORTH CENTRAL												
Minnesota	4	13	4	------	------	------	5	4	6	2	2	1
Iowa	0	4	4	------	------	------	4	1	8	0	1	1
Missouri	4	1	9	2	------	1	3	5	5	5	14	1
North Dakota	2	7	2	------	1	1	0	1	2	0	0	0
South Dakota	1	7	4	------	------	------	2	0	0	0	0	0
Nebraska	2	0	3	3	4	2	2	1	3	0	1	1
Kansas	7	4	3	------	2	1	3	6	4	1	2	1
SOUTH ATLANTIC												
Delaware	0	0	0	------	------	------	0	0	1	0	0	0
Maryland [2]	8	7	4	1	------	1	2	7	7	2	4	2
District of Columbia	0	2	1	------	------	------	0	1	1	1	1	0
Virginia	20	6	16	97	62	62	4	4	6	1	2	2
West Virginia	10	4	6	------	1	1	0	0	8	5	3	1
North Carolina	50	21	46	------	------	------	2	3	7	[3] 2	1	1
South Carolina	26	7	16	101	113	113	6	4	5	0	0	1
Georgia	31	14	26	11	7	6	1	5	5	3	0	0
Florida	6	10	7	------	2	2	1	8	2	1	1	0
EAST SOUTH CENTRAL												
Kentucky	9	11	11	1	1	1	9	0	4	0	4	0
Tennessee	39	12	13	6	5	12	3	3	3	3	1	1
Alabama	34	14	18	12	10	15	0	3	5	1	1	1
Mississippi [2]	25	19	13	------	------	------	------	------	------	1	1	1
WEST SOUTH CENTRAL												
Arkansas	6	6	6	------	21	10	5	2	2	1	1	0
Louisiana	9	13	8	34	------	1	4	2	3	1	2	1
Oklahoma	2	12	10	21	23	17	0	6	2	1	2	1
Texas	58	36	33	492	363	310	30	32	17	4	6	1
MOUNTAIN												
Montana	4	7	5	2	3	2	18	2	3	0	0	0
Idaho	1	0	0	1	------	------	17	1	4	0	0	0
Wyoming	0	0	0	------	3	3	2	1	2	0	0	0
Colorado	4	3	3	8	2	23	2	0	6	0	2	0
New Mexico	7	12	1	1	------	------	0	1	1	0	1	0
Arizona	5	1	1	4	34	30	3	2	8	1	1	0
Utah [2]	1	0	0	------	------	------	3	5	5	0	0	0
Nevada	0	0	0	------	------	------	1	0	0	0	0	0
PACIFIC												
Washington	8	8	2	------	1	1	49	14	11	1	2	2
Oregon	0	3	3	------	2	3	16	19	18	0	0	0
California	18	17	13	13	10	12	148	107	49	11	11	2
Total	467	325	336	847	695	728	540	416	626	83	122	39
38 weeks	10,217	8,077	8,926	75,069	341,582	171,545	104,125	593,495	541,518	[4] 6,578	13,729	2,623

[1] New York City only.
[2] Period ended earlier than Saturday.
[3] Corrections, week ended August 25, meningococcus meningitis: Massachusetts 2 cases (instead of 0); North Carolina 4 cases (instead of 5).

Telegraphic morbidity reports from State health officers for the week ended September 22, 1945, and comparison with corresponding week of 1944 and 5-year median—Con.

Division and State	Poliomyelitis			Scarlet fever			Smallpox			Typhoid and paratyphoid fever [4]		
	Week ended—		Median 1940–44	Week ended—		Median 1940–44	Week ended—		Median 1940–44	Week ended—		Median 1940–44
	Sept. 22, 1945	Sept. 23, 1944		Sept. 22, 1945	Sept. 23, 1944		Sept. 22, 1945	Sept. 23, 1944		Sept. 22, 1945	Sept. 23, 1944	
NEW ENGLAND												
Maine	9	6	1	12	24	7	0	0	0	0	0	0
New Hampshire	1	5	2	0	0	2	0	0	0	0	0	0
Vermont	5	8	2	2	0	3	0	0	0	0	0	0
Massachusetts	51	34	20	44	68	68	0	0	0	3	4	4
Rhode Island	1	1	1	5	8	4	0	0	0	0	0	0
Connecticut	11	17	10	7	9	9	0	0	0	1	1	1
MIDDLE ATLANTIC												
New York	110	383	57	82	59	85	0	0	0	4	8	11
New Jersey	55	40	17	15	21	21	0	0	0	2	2	2
Pennsylvania	48	82	14	76	56	72	0	0	0	5	7	17
EAST NORTH CENTRAL												
Ohio	37	77	34	95	71	79	0	1	0	4	8	8
Indiana	11	20	15	28	19	28	0	2	0	5	4	5
Illinois	93	38	50	62	78	73	0	0	0	5	3	9
Michigan [3]	12	75	28	40	49	58	0	0	0	3	4	8
Wisconsin	48	26	22	24	52	49	0	0	0	1	0	1
WEST NORTH CENTRAL												
Minnesota	23	45	23	26	26	26	0	0	0	1	1	1
Iowa	14	13	13	21	14	34	0	0	0	0	2	2
Missouri	9	15	10	22	35	27	0	0	0	1	6	9
North Dakota	0	3	2	6	5	4	0	0	0	0	0	0
South Dakota	1	1	1	0	1	9	0	0	0	0	1	0
Nebraska	14	3	10	16	3	7	0	0	0	2	0	0
Kansas	8	5	11	35	37	37	0	0	0	7	1	1
SOUTH ATLANTIC												
Delaware	2	8	1	2	1	1	0	0	0	0	1	1
Maryland [3]	[5] 13	31	3	22	11	14	0	0	0	5	1	4
District of Columbia	7	14	1	9	6	5	0	0	0	1	0	1
Virginia	19	48	4	32	45	28	0	0	0	7	4	10
West Virginia	3	18	6	42	44	37	0	0	0	1	6	6
North Carolina	14	23	7	48	44	62	0	0	0	2	0	6
South Carolina	6	2	2	22	6	6	0	0	0	4	5	5
Georgia	[5] 6	3	1	11	19	19	0	0	0	6	5	12
Florida	12	1	2	6	5	3	0	0	0	6	1	1
EAST SOUTH CENTRAL												
Kentucky	3	31	7	32	14	19	1	0	0	7	13	13
Tennessee	21	12	6	47	35	44	0	0	0	18	3	11
Alabama	4	1	1	18	27	27	0	0	0	3	0	4
Mississippi [3]	5	9	3	12	10	3	0	0	0	3	5	6
WEST SOUTH CENTRAL												
Arkansas	2	1	2	15	11	6	0	0	0	3	7	11
Louisiana	10	5	4	12	4	4	0	0	0	4	11	11
Oklahoma	15	2	3	8	6	6	0	0	0	5	1	7
Texas	39	5	5	56	28	19	0	0	0	17	16	17
MOUNTAIN												
Montana	7	8	2	6	5	5	0	0	0	5	0	0
Idaho	2	0	0	6	12	5	0	0	0	0	0	2
Wyoming	3	0	0	9	4	3	0	0	0	0	0	0
Colorado	11	2	4	7	10	10	0	0	0	5	2	6
New Mexico	1	1	1	7	3	3	0	0	0	8	6	4
Arizona	0	9	2	5	4	2	0	0	0	0	0	1
Utah [3]	22	0	2	3	4	4	0	0	0	0	0	0
Nevada	0	1	0	0	0	0	0	0	0	0	0	0
PACIFIC												
Washington	20	5	5	0	27	19	0	0	0	2	2	2
Oregon	2	12	12	14	28	6	1	0	0	0	4	1
California	54	9	9	108	80	66	0	0	0	11	3	4
Total	[5] 864	1,158	796	1,177	1,128	1,128	2	3	6	167	148	218
38 weeks	8,883	13,570	5,803	139,374	151,709	102,603	279	317	639	3,671	4,072	5,137

[3] Period ended earlier than Saturday.

[4] Including paratyphoid fever reported separately, as follows: Massachusetts 3; New York 1; Ohio 1; Indiana 1; Michigan 1; Maryland 1; Virginia 1; South Carolina 2; Georgia 1; Louisiana 1; Texas 2; New Mexico 1; California 1.

[5] Delayed reports, included in cumulative total only, poliomyelitis: Maryland, July, 1 case; Georgia, August, 8 cases.

Telegraphic morbidity reports from State health officers for the week ended September 22, 1945, and comparison with corresponding week of 1944 and 5-year median—Con.

Division and State	Whooping cough: Week ended— Sept. 22, 1945	Whooping cough: Week ended— Sept. 23, 1944	Whooping cough: Median 1940–44	Week ended Sept. 22, 1945: Dysentery: Amebic	Dysentery: Bacillary	Dysentery: Unspecified	Encephalitis, infectious	Rocky Mt. spotted fever	Tularemia	Typhus fever, endemic	Undulant fever
NEW ENGLAND											
Maine	39	3	12	0	0	0	0	0	0	0	1
New Hampshire	0	0	2	0	0	0	0	0	0	0	1
Vermont	11	20	17	0	0	0	0	0	0	0	2
Massachusetts	138	79	123	0	0	5	1	0	0	0	1
Rhode Island	18	11	32	0	0	0	0	0	0	0	0
Connecticut	34	33	34	0	5	0	1	0	0	0	3
MIDDLE ATLANTIC											
New York	286	119	266	2	44	0	2	0	0	1	5
New Jersey	151	68	120	0	1	0	0	0	0	0	1
Pennsylvania	191	82	205	0	1	0	0	0	0	0	3
EAST NORTH CENTRAL											
Ohio	153	110	220	0	0	5	0	0	0	0	0
Indiana	20	10	18	2	0	3	1	0	0	0	1
Illinois	79	115	146	5	0	0	1	0	2	0	4
Michigan [3]	179	97	263	1	7	1	0	0	0	0	3
Wisconsin	47	145	199	0	0	0	0	0	0	0	6
WEST NORTH CENTRAL											
Minnesota	28	40	40	3	0	0	0	0	0	0	6
Iowa	3	15	21	0	0	0	0	0	0	0	3
Missouri	21	9	12	0	0	0	0	0	0	0	0
North Dakota	0	6	10	0	0	0	0	0	0	0	1
South Dakota	1	3	3	0	0	0	0	0	0	0	0
Nebraska	1	3	8	0	0	0	0	0	0	0	0
Kansas	20	19	33	0	0	0	1	0	0	0	8
SOUTH ATLANTIC											
Delaware	0	0	2	0	0	0	0	0	0	0	0
Maryland [3]	37	53	69	0	0	13	0	0	0	0	0
District of Columbia	7	1	13	0	0	0	0	0	0	0	0
Virginia	18	18	34	0	0	336	0	0	0	0	1
West Virginia	3	5	22	0	0	0	0	0	0	0	0
North Carolina	77	141	60	0	0	0	0	2	0	4	0
South Carolina	49	25	37	4	56	0	0	0	0	3	0
Georgia	15	20	16	0	3	1	0	0	2	19	4
Florida	4	29	13	1	2	0	0	0	0	7	0
EAST SOUTH CENTRAL											
Kentucky	81	58	58	0	0	0	0	0	0	0	0
Tennessee	20	32	32	1	0	2	0	0	3	3	4
Alabama	2	14	14	3	0	0	0	0	0	17	1
Mississippi [3]	------	------	------	0	0	0	0	0	0	4	2
WEST SOUTH CENTRAL											
Arkansas	6	30	13	0	7	0	0	0	4	2	1
Louisiana	28	0	1	0	2	0	0	0	0	16	5
Oklahoma	14	7	5	0	8	0	0	4	0	0	2
Texas	127	108	108	6	690	6	0	0	1	76	7
MOUNTAIN											
Montana	8	54	23	0	0	0	0	0	0	0	0
Idaho	11	0	2	0	0	6	0	0	0	0	0
Wyoming	2	6	7	0	0	0	0	0	0	0	0
Colorado	32	10	35	0	0	0	0	0	0	0	0
New Mexico	11	3	9	0	9	3	0	0	0	0	0
Arizona	17	16	13	0	0	12	0	0	0	0	0
Utah [3]	12	20	27	0	0	0	0	0	0	0	1
Nevada	0	0	0	0	0	0	0	0	0	0	0
PACIFIC											
Washington	16	11	34	0	0	0	0	0	0	0	3
Oregon	13	8	8	0	0	4	0	0	0	0	0
California	187	81	170	2	7	0	24	0	0	0	7
Total	2,217	1,737	2,722	30	842	397	31	6	12	152	87
Same week 1944	1,737	------	------	30	561	322	19	14	11	159	56
Average, 1942–44	2,438	------	------	35	482	248	17	[6] 4	10	[6] 146	------
38 weeks: 1945	95,586	------		1,383	19,610	8,342	455	420	576	3,508	3,521
1944	71,887	------	------	1,275	16,656	6,643	491	430	430	3,600	2,653
Average, 1942–44	118,050	------	[6] 136,936	1,235	12,809	5,995	484	[6] 427	598	[6] 2,511	------

[3] Period ended earlier than Saturday.
[6] 5-year median, 1940–44.

WEEKLY REPORTS FROM CITIES

City reports for week ended September 15, 1945

This table lists the reports from 85 cities of more than 10,000 population distributed throughout the United States, and represents a cross section of the current urban incidence of the diseases included in the table.

	Diphtheria cases	Encephalitis, infectious, cases	Influenza		Measles cases	Meningitis, meningococcus, cases	Pneumonia deaths	Poliomyelitis cases	Scarlet fever cases	Smallpox cases	Typhoid and paratyphoid fever cases	Whooping cough cases
			Cases	Deaths								
NEW ENGLAND												
Maine:												
Portland	1	0	------	0	1	1	1	2	0	0	0	8
New Hampshire:												
Concord	0	0	------	0	0	0	0	0	1	0	0	0
Vermont:												
Barre	0	0	------	0	0	0	0	1	0	0	0	0
Massachusetts:												
Boston	1	0	------	0	4	0	3	14	12	0	0	22
Fall River	0	0	------	0	0	0	0	0	1	0	0	2
Springfield	0	0	1	0	0	0	1	0	2	0	0	3
Worcester	0	0	------	0	6	0	8	0	1	0	0	5
Rhode Island:												
Providence	0	0	------	0	1	0	2	0	2	0	0	13
Connecticut:												
Bridgeport	0	0	------	0	0	0	0	2	0	0	0	0
Hartford	0	0	------	0	0	0	0	2	1	0	0	7
New Haven	0	0	------	0	0	0	1	1	0	0	0	5
MIDDLE ATLANTIC												
New York:												
Buffalo	1	0	------	0	1	0	5	8	5	0	0	8
New York	8	3	1	0	9	5	43	49	18	0	4	165
Rochester	0	0	------	0	4	0	3	10	0	0	0	21
Syracuse	0	0	------	0	0	0	0	0	1	0	0	38
New Jersey:												
Camden	0	0	------	0	1	0	1	1	0	0	0	3
Newark	0	0	------	0	1	0	0	3	2	0	1	11
Trenton	0	0	------	0	0	0	1	4	0	0	1	2
Pennsylvania:												
Philadelphia	0	0	1	0	18	1	17	25	11	0	1	101
Pittsburgh	0	0	------	0	1	0	8	10	5	0	1	6
Reading	0	0	------	0	0	1	1	1	2	0	0	1
EAST NORTH CENTRAL												
Ohio:												
Cincinnati	0	0	------	1	1	0	7	0	6	0	0	5
Cleveland	1	0	1	0	1	1	8	4	7	0	0	41
Columbus	0	0	------	0	0	0	1	0	7	0	1	2
Indiana:												
Fort Wayne	0	0	------	0	0	0	1	1	0	0	0	2
Indianapolis	2	0	------	0	1	0	6	1	3	0	0	0
Terre Haute	0	0	------	0	0	0	3	0	0	0	0	0
Illinois:												
Chicago	0	0	------	0	27	6	17	18	11	0	0	68
Springfield	0	0	------	0	0	0	2	0	0	0	0	0
Michigan:												
Detroit	4	0	------	0	13	1	6	1	12	0	0	92
Flint	0	0	------	0	8	0	0	0	1	0	0	0
Grand Rapids	0	0	------	0	0	0	0	0	1	0	0	0
Wisconsin:												
Kenosha	0	0	------	0	0	0	0	0	0	0	0	0
Milwaukee	0	0	------	0	5	0	0	16	4	0	0	4
Racine	0	0	------	0	0	0	0	0	1	0	0	7
Superior	0	0	------	0	1	0	0	0	0	0	0	2
WEST NORTH CENTRAL												
Minnesota:												
Duluth	0	0	------	1	1	0	0	0	3	0	0	0
Minneapolis	0	0	------	0	1	0	2	15	2	0	1	9
Missouri:												
Kansas City	1	0	------	------	1	0	2	2	4	0	0	8
St. Joseph	0	0	1	------	1	1	0	0	0	0	0	0
St. Louis	1	0	------	1	1	3	5	16	6	0	1	9

City reports for week ended September 15, 1945—Continued

	Diphtheria cases	Encephalitis, infectious cases	Influenza		Measles cases	Meningitis, meningococcus, cases	Pneumonia deaths	Poliomyelitis cases	Scarlet fever cases	Smallpox cases	Typhoid and paratyphoid fever cases	Whooping cough cases
			Cases	Deaths								
WEST NORTH CENTRAL—continued												
Nebraska:												
Omaha	0	0	------	0	0	0	1	15	0	0	0	1
Kansas:												
Topeka	0	0	------	0	1	0	0	0	0	0	0	8
Wichita	0	0	------	0	0	0	9	1	4	0	0	7
SOUTH ATLANTIC												
Delaware:												
Wilmington	0	0	------	0	0	0	0	0	0	0	0	3
Maryland:												
Baltimore	6	0	------	0	0	0	6	2	12	0	0	33
Cumberland	0	0	------	0	0	0	0	0	2	0	0	0
Frederick	0	0	------	0	0	0	0	0	0	0	0	0
District of Columbia:												
Washington	0	0	------	0	2	0	2	5	4	0	0	6
Virginia:												
Lynchburg	0	0	------	0	0	0	3	0	3	0	0	3
Richmond	0	0	------	0	0	1	3	12	5	0	0	2
Roanoke	0	0	------	0	0	0	0	0	0	0	0	1
West Virginia:												
Wheeling	1	0	------	0	0	0	1	0	1	0	0	0
North Carolina:												
Wilmington	1	0	------	0	0	0	0	0	0	0	0	8
Winston-Salem	0	0	------	0	0	0	2	0	1	0	0	6
South Carolina:												
Charleston	0	0	------	0	0	0	1	0	0	0	0	0
Georgia:												
Atlanta	1	0	4	0	0	0	3	0	0	0	1	6
Brunswick	0	0	------	0	0	0	1	0	0	0	0	0
Savannah	0	0	------	0	0	1	0	0	1	0	0	0
Florida:												
Tampa	0	0	------	1	0	0	0	0	2	0	0	0
EAST SOUTH CENTRAL												
Tennessee:												
Memphis	0	0	------	0	0	1	4	3	0	0	1	3
Nashville	0	0	------	0	0	0	3	2	0	0	0	0
Alabama:												
Birmingham	2	0	------	0	0	0	2	2	0	0	0	0
Mobile	0	0	------	0	0	0	0	0	0	0	0	0
WEST SOUTH CENTRAL												
Arkansas:												
Little Rock	0	0	------	0	0	0	0	0	1	0	0	0
Louisiana:												
New Orleans	5	0	------	1	0	2	8	6	2	0	2	0
Shreveport	4	0	------	0	0	0	3	1	4	0	0	0
Texas:												
Dallas	2	0	------	0	1	0	4	1	4	0	0	0
Galveston	0	0	------	0	0	0	0	0	1	0	0	0
Houston	1	0	------	0	0	1	3	3	0	0	0	0
San Antonio	1	0	1	1	0	0	4	3	3	0	0	1
MOUNTAIN												
Montana:												
Billings	0	0	------	0	0	0	0	2	0	0	0	0
Great Falls	0	0	------	0	0	0	0	1	1	0	0	0
Helena	0	0	------	0	0	0	0	0	0	0	0	0
Missoula	0	0	------	0	0	0	1	0	0	0	0	0
Idaho:												
Boise	0	0	------	0	0	0	0	0	0	0	0	2
Colorado:												
Denver	1	1	1	0	3	1	0	15	3	0	0	13
Pueblo	0	0	------	0	0	0	0	2	1	0	0	3
Utah:												
Salt Lake City	0	0	------	0	2	0	1	11	2	0	0	3

City reports for week ended September 15, 1945—Continued

	Diphtheria cases	Encephalitis, infectious, cases	Influenza		Measles cases	Meningitis, meningococcus, cases	Pneumonia deaths	Poliomyelitis cases	Scarlet fever cases	Smallpox cases	Typhoid and paratyphoid fever cases	Whooping cough cases
			Cases	Deaths								
PACIFIC												
Washington:												
Seattle	0	0		0	22	0	4	2	3	0	0	10
Spokane	0	0		0	0	0	1	0	0	0	0	0
Tacoma	0	0		0	5	0	1	0	0	0	0	1
California:												
Los Angeles	1	0	5	0	9	0	2	10	15	0	1	22
Sacramento	0	0		0	0	1	2	1	1	0	0	11
San Francisco	1	0		0	19	3	8	7	5	0	1	2
Total	47	4	16	6	173	31	238	314	213	0	17	825
Corresponding week, 1944	49		13	6	90		206		219	0	31	650
Average, 1940-44	51		33	[1] 9	[2] 147		[1] 225		266	0	37	904

[1] 3-year average, 1942-44.
[2] 5-year median, 1940-44.

Dysentery, amebic.—Cases: New York 4; Topeka 1; Baltimore 4; Spokane 2; San Francisco 1.

Dysentery, bacillary.—Cases: Buffalo 1; New York 8; Detroit 6; Lynchburg 1; Charleston, S. C. 5; Los Angeles 2.

Dysentery, unspecified.—Cases: Baltimore 3; Richmond 2; San Antonio 8.

Rocky Mountain spotted fever.—Cases: Cincinnati 1; Richmond 3.

Typhus fever, endemic.—Cases: New York 1; Charleston, S. C. 2; Atlanta 4; Savannah 6; Birmingham 4; Memphis 1; Mobile 3; New Orleans 5; Dallas 1; Houston 7; San Antonio 7; Los Angeles 1.

Rates (annual basis) per 100,000 population, by geographic groups, for the 85 cities in the preceding table (estimated population, 1943, 33,858,300)

	Diphtheria case rates	Encephalitis, infectious, case rates	Influenza		Measles case rates	Meningitis, meningococcus, case rates	Pneumonia death rates	Poliomyelitis case rates	Scarlet fever case rates	Smallpox case rates	Typhoid and paratyphoid fever case rates	Whooping cough case rates
			Case rates	Death rates								
New England	5.2	0.0	2.6	0.0	31	2.6	41.8	57.5	52	0.0	0.0	170
Middle Atlantic	4.2	1.4	0.9	0.0	16	3.2	36.5	51.4	20	0.0	3.7	165
East North Central	4.3	0.0	0.6	0.6	35	4.9	31.4	25.2	33	0.0	0.6	137
West North Central	4.5	0.0	2.3	4.5	14	9.0	42.8	110.4	43	0.0	4.5	95
South Atlantic	15.3	0.0	6.8	1.7	3	3.4	37.4	32.3	53	0.0	1.7	115
East South Central	11.8	0.0	0.0	0.0	0	5.9	53.1	41.3	0	0.0	5.9	18
West South Central	37.3	0.0	2.9	5.7	3	8.6	63.1	40.2	43	0.0	5.7	3
Mountain	7.9	7.9	7.9	0.0	40	7.9	15.9	246.2	56	0.0	0.0	167
Pacific	3.2	0.0	7.9	0.0	87	6.3	28.5	31.6	38	0.0	3.2	73
Total	7.3	0.6	2.5	0.9	27	4.8	36.8	48.5	33	0.0	2.6	127

PLAGUE INFECTION IN KERN AND SANTA CLARA COUNTIES, CALIF.

Under date of September 14, plague infection was reported proved on September 12 in tissue and fleas from ground squirrels, *C. beecheyi*, shot in Kern and Santa Clara Counties, Calif., as follows: *Kern County*—pool of 200 fleas from 13 ground squirrels shot 2 miles south and 1½ miles west of Cummings Valley School; *Santa Clara County*—pool of 400 fleas from 80 ground squirrels shot 16 miles southeast of Gilroy, and tissue from 1 ground squirrel and a pool of 200 fleas from 13 ground squirrels shot 6½ miles east and 2 miles south of Gilroy. Under date of September 17 plague infection was reported proved on September 13 in tissue from 2 ground squirrels, *C. beecheyi*, shot 16 miles southeast of Gilroy.

TERRITORIES AND POSSESSIONS

Puerto Rico

Notifiable diseases—4 weeks ended September 8, 1945.—During the 4 weeks ended September 8, 1945, cases of certain notifiable diseases were reported in Puerto Rico as follows:

Disease	Cases	Disease	Cases
Bilharziasis	3	Ophthalmia neonatorum	2
Cerebrospinal meningitis	1	Puerperal fever	2
Chickenpox	25	Ringworm	1
Diphtheria	62	Syphilis	246
Dysentery, unspecified	13	Tetanus	8
Filariasis	2	Tetanus, infantile	3
Gonorrhea	214	Trachoma	1
Influenza	31	Tuberculosis (all forms)	556
Leprosy	1	Typhoid and paratyphoid fever	9
Malaria	264	Typhus fever (murine)	31
Measles	13	Whooping cough	51
Mumps	2		

FOREIGN REPORTS

CANADA

Provinces—Communicable diseases—Week ended September 1, 1945—During the week ended September 1, 1945, cases of certain communicable diseases were reported by the Dominion Bureau of Statistics of Canada as follows:

Disease	Prince Edward Island	Nova Scotia	New Brunswick	Quebec	Ontario	Manitoba	Saskatchewan	Alberta	British Columbia	Total
Chickenpox				16	34	7	13	19	9	98
Diphtheria	3	4	3	46	6	4	1			67
Dysentery:										
Amebic					2					2
Bacillary				19					6	25
Encephalitis, infectious							1			1
German measles					1	1		3	2	7
Influenza		8			14				2	24
Measles			1	18	20		2	5	5	51
Meningitis, meningococcus				1			1	1		3
Mumps				12	14	10	5	12	8	61
Poliomyelitis		3	1	7	17	1	1			30
Scarlet fever		1	4		18	12	7	12	4	58
Tuberculosis (all forms)		9	4	148	28	12	1	2	19	223
Typhoid and paratyphoid fever		1		7		2		1	1	12
Undulant fever				1	1		1	1	1	5
Venereal diseases:										
Gonorrhea	1	18	36	141	223	68	29	50	74	640
Syphilis		10	5	82	94	16	4	9	43	263
Other forms				1						1
Whooping cough		1	22	147	11	6	3	19	2	211

REPORTS OF CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER RECEIVED DURING THE CURRENT WEEK

NOTE.—Except in cases of unusual incidence, only those places are included which had not previously reported any of the above-mentioned diseases, except yellow fever, during the current year. All reports of yellow fever are published currently.

A table showing the accumulated figures for these diseases for the year to date is published in the PUBLIC HEALTH REPORTS for the last Friday in each month.

Plague

Ecuador.—For the month of August 1945, plague infection was reported in Ecuador as follows: Canar Province, 2 cases, 1 death; Loja Province, 5 cases, 2 deaths.

Great Britain—Malta.—For the week ended September 8, 1945, 13 cases of plague were reported in Malta. For the week ended September 15, 1945, 5 cases of plague were reported in Malta, including 2 cases in Marsa, 2 cases in Zurrie, and 1 fatal case in Hamrun.

Italy—Sicily—Palermo.—On September 19, 1945, 4 cases of plague with 3 deaths were reported in Palermo, Sicily, Italy.[1]

Morocco (French).—For the period September 1–10, 1945, 6 cases of plague were reported in French Morocco.

Smallpox

Belgian Congo.—For the week ended August 25, 1945, 107 cases of smallpox were reported in Belgian Congo.

British East Africa.—For the week ended September 15, 1945, 91 cases of smallpox with 9 deaths were reported in Kenya, and for the week ended August 11, 1945, 160 cases of smallpox with 26 deaths were reported in Tanganyika, British East Africa.

Rhodesia, Northern.—For the week ended August 4, 1945, 638 cases of smallpox with 2 deaths were reported in Northern Rhodesia.

Typhus Fever

Algeria.—For the period August 11–20, 1945, 29 cases of typhus fever, including 3 cases in Algiers, and 1 case in Oran, were reported in Algeria.

Ecuador.—For the month of August 1945, 95 cases of typhus fever with 3 deaths were reported in Ecuador, including 43 cases with 2 deaths reported in Quito, 19 cases reported in Ibarra, and 11 cases reported in Ambato.

Morocco (French).—For the period September 1–10, 1945, 88 cases of typhus fever, including 65 cases reported in Casablanca region and 3 cases in the city of Casablanca, were reported in French Morocco.

[1] For recent report of plague in Taranto, Italy, see PUB. HEALTH REP., Oct. 5, 1945, p. 1197.

INDUSTRIAL MANGANESE POISONING [1]

A Review

This bulletin discusses the occurrence and uses of manganese, its physicochemical properties, its analytical evaluation, industrial exposure, toxicology, the treatment of manganese poisoning, the maximum permissible exposure in industry, and measures for the prevention of industrial manganese poisoning.

All the known cases of manganese poisoning which have been reported since its discovery by Couper in 1837 have been collected and tabulated through 1940. These total 353 and reference is made to the original papers describing these cases.

The great majority of reported cases of manganese poisoning have occurred in grinders of manganese ores in which the condition could be associated with the dusty work of sorting, drying, grinding, and sifting. However, manganese poisoning from manganese fume has been reported in the case of electric welders who used electrodes containing this metal.

The symptoms of industrial manganese poisoning, differential diagnosis of chronic poisoning, pathology of poisoning in man, the laboratory examinations, absorption, and elimination of manganese, and prognosis have received particular attention in this bulletin. The importance of recognition of manganese poisoning at an early stage is stressed.

A comprehensive bibliography of 201 references to the original literature is given.

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[1] Industrial manganese poisoning. By Lawrence T. Fairhall and Paul A. Neal. National Institute of Health Bulletin No. 182. Government Printing Office, 1943. For sale by the Superintendent of Documents, Washington 25, D. C. Price 10 cents.

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FEDERAL SECURITY AGENCY

UNITED STATES PUBLIC HEALTH SERVICE

THOMAS PARRAN, *Surgeon General*

DIVISION OF PUBLIC HEALTH METHODS

G. ST. J. PERROTT, *Chief of Division*

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It contains (1) current information regarding the prevalence and geographic distribution of communicable diseases in the United States, insofar as data are obtainable, and of cholera, plague, smallpox, typhus fever, yellow fever, and other important communicable diseases throughout the world; (2) articles relating to the cause, prevention, and control of disease; (3) other pertinent information regarding sanitation and the conservation of the public health.

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